

United States Patent [19]

Tin

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[54] VESICLE STABILIZATION

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[56] References Cited

U.S. PATENT DOCUMENTS

3,527,712 9/1970 Renn et al. 252/315.3 X
3,619,842 11/1971 Maierson 428/402.2 X
4,185,618 1/1980 Corey 514/944 X
4,217,344 8/1980 Vanlerberghe et al. 264/4.1 X
4,235,871 11/1980 Papahadjopoulos et al. 264/4.6 X
4,310,506 1/1982 Baldeschwieler et al. 264/4.1 X
4,439,488 3/1984 Trimmell et al. 424/418 X
4,493,894 1/1985 Miyashiro et al. 435/101 X

FOREIGN PATENT DOCUMENTS

0069307 6/1982 European Pat. Off. .
0160266 4/1984 European Pat. Off. .
8311716 7/1983 France .
8503640 8/1985 PCT Int'l Appl. .

OTHER PUBLICATIONS

"Carbopol Scales Up", Chemistry and Engineering News, 36, 64 & 65, Sep. 29, 1958.
The United States Pharmacopoeia-National Formulary Monograph, 1985, p. 1542.
Mauk et al., "Preparation of Lipid Vesicles Containing High Levels of Entrapped Radioactive Cations", Analytical Biochemistry, vol. 94, pp. 302-307, (1979).
Mauk et al., "Stability of Lipid Vesicles in Tissues of the

Mouse", Proc. Natl. Acad. Sci. U.S.A., vol. 76, No. 2, pp. 765-769, (1979).

Frokjaer et al., "Stability and Storage of Liposomes", in Optimization of Drug Delivery, Alfred Benzon Symposium, 17, Bundgaard et al., Eds., Munksgaard, Copenhagen, pp. 384-397, (1982).

Weinstein et al., "Liposomes and Local Hyperthermia", Science, vol. 204, pp. 188-191, (1979).

Sheetz et al., "Effect of Sonication on the Structure of Lecithin Bilayers", Biochemistry, vol. 11, No. 24, pp. 4573-4581, (1972).

Lawaczeck et al., "The Formation and Annealing of Structural Defects in Lipid Bilayer Vesicles", Biochimica et Biophysica Acta, vol. 443, pp. 313-330, (1976).

Schullery et al., "Fusion of Dipalmitoyl Phosphatidylcholine Vesicles", Biochemistry, vol. 19, pp. 3919-3923, (1980).

Abra et al., "Liposome Disposition in Vivo", Biochimica et Biophysica Acta, vol. 666, pp. 493-503, (1981).

Kao et al., "Interactions of Liposomes with the Reticuloendothelial System", Biochimica et Biophysica Acta, vol. 677, pp. 453-461, (1981).

Ryman et al., "Potential Applications of Liposomes to Therapy", Annals N.Y. Acad. Sci., vol. 308, pp. 281-307, (1978).

Fendler, "Surfactant Vesicles as Membrane Mimetic Agents", Acc. Chem. Res., vol. 13, pp. 7-13, (1980).

Chemical Abstracts No. 188 156K (vol. 97, No. 22, Nov. 29, 1982).

Chemical Abstracts No. 187329V, (vol. 94, No. 23, Jun. 8, 1981).

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[57] ABSTRACT

The present invention relates to a process of stabilizing micellar particles such as vesicles and increasing the shelf life by suspending the particles in a polymeric gel matrix. The invention also relates to such particles suspended in the gel matrix with a protective gel surface thereabout which is capable of becoming fluid and converting the protective surface of an aqueous suspension.

12 Claims, 1 Drawing Sheet